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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,980	08/22/2003	Chung K. Chu	G25-078	1065

7590 09/26/2005

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,980	CHU ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *March 03, 2004*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant has cancelled claims 1-19. Claims 20-39 are pending.

Election/Restrictions

The examiner, in light of the preliminary amendment filed by Applicant on August 22, 2003, has vacated the restriction requirement mailed on July 7, 2005.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. Examiner suggests inserting the word "that" between the words "such" and "the" on page 9 line 12 of the specification.

Claim 39 is objected to because of the following informalities: the end of claim 39 has two periods. Appropriate correction is required.

Claim Rejections - 35 USC § 112

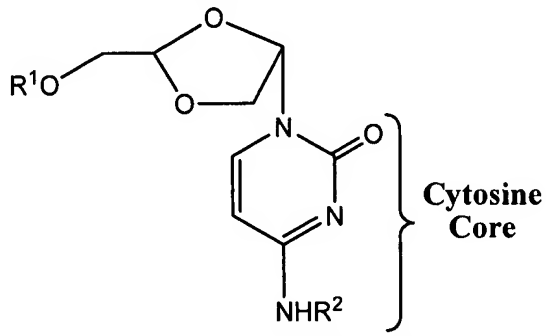
The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of leukemia, colon tumors, melanoma, and CNS, ovarian, renal, prostate, breast, and non-small cell lung cancers, wherein R_1 and R_2 of the administered pharmaceutical are both hydrogen ((-)-OddC), does not reasonably provide enablement for head and neck, bladder, uterine, and small cell lung cancers (c.f.

Examples 9 and 10, Table 2, and the structure shown below). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification lacks

Compounds of the Instant Invention



data and specific examples regarding the treatment of head and neck, bladder, uterine, and small cell lung cancers as well as treatments of leukemia, colon tumors, melanoma, and CNS, ovarian, renal, prostate, breast, and non-small cell lung cancers, wherein R_1 and R_2 of the administered pharmaceutical are **not hydrogen**. These cancers have dissimilar points of origins in the body and involve the development of malignancy in different cell types. Therefore, a person of ordinary skill in the art would expect that the drugs used to treat these diseases would exhibit different mechanisms of action and degrees of success in the treatment of these maladies. For these reasons, appropriate treatments for dissimilar kinds of cancer are expected to be different and no single treatment is known in the art that can be used universally to treat all cancers with a reasonable expectation of success. Additional Wands analysis of these claims follows.

The rejected claims are broad because they encompass the treatment of a wide range of cancers resulting from the malignancy of different organs and cell types (e.g. ovaries, prostate, non-small cells of the lung, etc.). For example, the term "head and neck cancer" encompasses cancers occurring in the regions of the head and neck, including glandular cancers (e.g. thyroid)

cancers localized in the tissues of the mouth and throat, as well as brain cancer, etc. The term lung cancer encompasses cancers associated with small cells and non-small cells found in the lungs. Applicant does not provide further guidance as to which sub-types of cancer are treated by the instant invention.

The invention relates to a class of compounds based on a dioxalane-derivatized cytosine core structure administered to patients (animals and humans) to treat cancer (see structure on page 3 of this office action). This core structure consists of two sites of derivation, R_1 and R_2, which may correspond independently to at least 64 different substituents. The number of compounds encompassed by this core structure is estimated to be ~128 factorial (i.e. ~3.8×10^{215} compounds). It is noted that the examples provided by the applicant regarding the treatment of different cancers/tumors only relate to a compound in which **both R_1 and R_2 are hydrogen (i.e. the compound abbreviated as (-)-OddC).** This compound represents **one species in an extremely large genus**.

The state of the art at the time of the instant invention regarding cytosine derivatives used as chemotherapeutics to treat cancer follows. Cytosine is considered a member of a class of compounds called nucleosides, which are glycoside (i.e. monosaccharide) derivatives of nucleic acids. Applicant's admission of prior art includes statements referring to the use of structurally distinct nucleoside derivatives to treat different cancers and their mechanism of action. For example, on pages 4 and 5 of the specification, Applicant cites two examples that are cytosine derivatives, cytosine arabinoside (Cytosar) and 5-azacytidine. Cytosine arabinoside is thought to act by the inhibition of nuclear DNA synthesis and is used primarily to treat acute myeloid leukemia. The second cytosine derivative, 5-azacytidine is used to treat acute myelocytic

leukemia and myelodysplastic syndrome and its mechanism of action is not mentioned. It is assumed that 5-azacytidine may have a mechanism of action similar to that of cytosine arabinoside. Cytosar is used also as an active agent to treat lymphocytic leukemia, and "to a lesser extent chronic myelocytic leukemia and non-Hodgkin's lymphoma." The chemotherapeutics with a cytosine structure known in the art at the time of the instant invention were used to treat a limited number of cancers, including acute myelocytic leukemia, lymphocytic leukemia, and non-Hodgkin's lymphoma. Dvonch et al. provide another example of a cytosine-based chemotherapeutic (*Cancer Research*, **1966**, *26*, 2386-2389) from the prior art that is described as the periodate oxidation product of cytidine (a nucleoside consisting of cytosine and an attached ribose sugar). This cytosine-based therapeutic was found to have activity against Leukemia 1210, yet exhibited no activity against Sarcoma 180 nor Adenocarcinoma 755. At the time of the instant invention the list of cancers treated by administration of cytosine-based chemotherapeutics modified to have a dioxalane substituent **did not** include the following: colon tumors, melanoma, CNS, ovarian, renal, prostate, breast, non-small cell lung, head and neck, bladder, uterine, and small cell lung cancers.

A person of ordinary skill in the art at the time of the instant invention is considered to be an actively practicing physician, pharmacist, or other health field professional having the appropriate training and medical background to prescribe drugs and/or know which drugs are effectively used in the treatment of specific kinds of cancer. These artisans all possess professional and/or advanced degrees (M.D., Pharm. D., and/or Ph. D.). Therefore, there is a high level of skill in the art.

The pharmaceutical art has a high level of unpredictability as it involves regulating and affecting physiological properties controlled and affected by different processes and agents (e.g. hormones, enzymes, DNA, etc.). The structure function relationship of chemotherapeutics cannot be predicted easily as a drug's effectiveness is affected by many variables, such as drug's bioavailabilty, mode of action, toxicity, as well as by the patient's general health, age, gender, and in the case of cancer treatment the stage of cancer at which treatment is begun. Regarding the instant invention, Applicant only provides examples of treatment of certain cancers (mentioned above) by the administration of compounds (see the general structure shown above on page 3) to a patient wherein R_1 and R_2 are hydrogen. However, R_1 and R_2 also can pertain to a wide variety of acyl substituents wherein the non-carbonyl moiety may range, for example, from a methyl group to a large 18-carbon cyclic group. These different substituents correspond to compounds that a person of ordinary skill in the art would expect to exhibit drastic differences in solubility under physiological conditions, bioavailability, hydrophobicity, polarity, therapeutic effectiveness, molecular size, and steric bulk. It is expected that a therapeutic agent having stericly large moieties at positions R_1 and/or R_2 would not be able to access the same receptor or enzyme active sites as the compound where R_1 and R_2 are both hydrogen. The replacement of hydrogen at position R_1 for an alkyl or other carbon group would reduce the hydrogen-bonding ability of this molecule and would be expected to affect its ability to interact with receptors and enzymes. Replacement of hydrogen at R_2 also would be expected to reduce the hydrogen bonding capability of the chemotherapeutic. A reduction in the hydrogen bonding ability of a chemotherapeutic agent would affect its solubility and intermolecular interactions, because hydrogen bonding is one of the stronger intermolecular interactions that can occur between

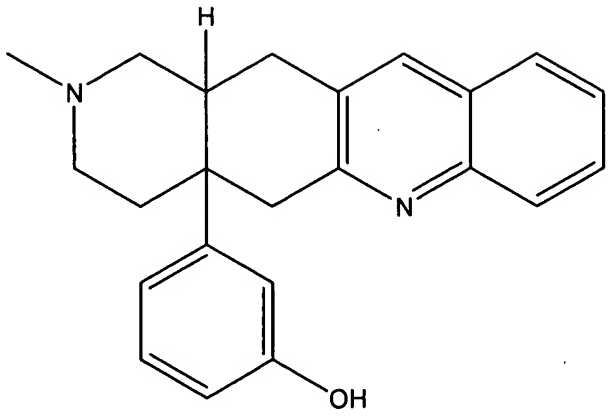
molecules. Changes in the intermolecular interactions will affect a compound's solubility in solvents and the degree to which it may interact with other molecules (see Brown, T. L. *et al. Chemistry: The Central Science, 6th ed.*, Prentice Hall: Englewood Cliffs, NJ, 1994, pp 373-381 and 459-461). The unpredictability in the pharmaceutical arts, especially drug discovery, is illustrated by the following discussion.

Drug discovery remains extremely tedious, laborious and expensive. For example, it is not all that uncommon for a pharmaceutical company to spend over one billion dollars in research and development, as well as clinical testing, before even a single drug sees the light of day in the marketplace, only then allowing said company the opportunity to begin recouping their investments for not only the successful drug, but also the countless other drugs that failed. Despite recent advancements in the sophistication of drug discovery instrumentation and techniques, an extraordinary degree of unpredictability remains in the biotechnology, chemical and pharmaceutical arts, requiring continued trial and error experimental research. The basis for the extraordinary degree of unpredictability associated with drug discovery in particular can be attributed to the exquisite stereospecificity that exists between an enzyme and its corresponding substrate, or a ligand and its corresponding receptor. This principle is particularly evidenced by the following examples previously documented in the biotechnology, chemical and pharmaceutical scientific literature and prior art.

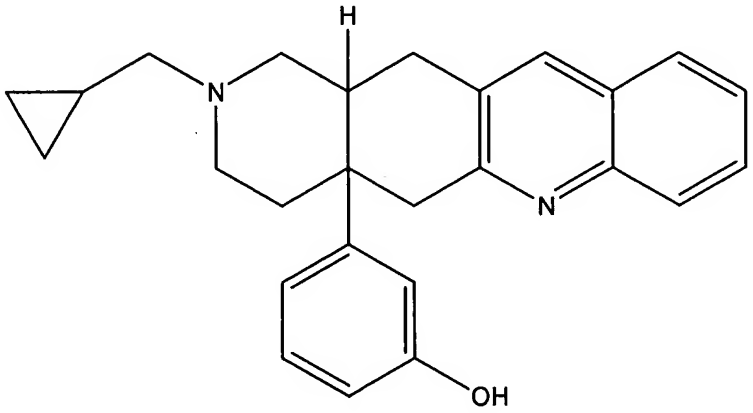
It is known in the biotechnology art that aminoacyl-tRNA synthetases exhibit an extremely high degree of stereospecificity with respect to their ability to discriminate between D- and L-optical isomers and between amino acids that are simple one carbon homologs of one another (i.e., aspartic acid versus glutamic acid), as well as between amino acids that are simply

molecular isomers (i.e., leucine versus isoleucine)." Francklyn, C., Aminoacyl-tRNA Synthetases: Versatile Players in the Changing Theater of Translation, **2002**, *RNA*, *8*, pp. 1363-1372. It is also known that vertebrate growth hormone, which consists of 198 amino acids in length, transforms from being an agonist to an antagonist when a single amino acid is changed. See U.S. Patent Number 5,350,836, which issued to Kopchick, et al. on September 27, 1994. It is further known that a majority of key therapeutics specifically act on particular cell surface receptors, for example: migraine drugs act on dopaminergic receptors; allergy drugs act on histamine receptors; asthma and blood pressure drugs act on adrenergic receptors; anti-depressive and anti-compulsive drugs act on serotonin receptors; and anti-anxiety drugs act on both serotonin receptors, as well as GABA receptors. For a general overview of the aforementioned cell surface receptors, see the relevant chapters and subheadings within Goodman & Gilman's *The Pharmacological Basis of Therapeutics, 9th Ed.*, McGraw-Hill, NY, 1996.

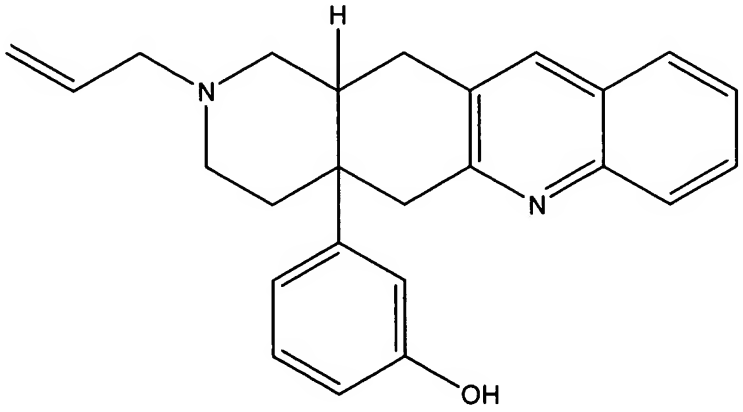
The unpredictable and surprisingly dramatic effects that can result from a simple modification of even a single pendant chemical moiety of an active core compound is strikingly apparent when considering opioid analgesics, for example. Upon simple substitution of the N-methyl group of TAN-67 (shown below), which is a highly selective and potent nonpeptidic δ opioid receptor *agonist*, with either a methylcyclopropyl group, or even an allyl group for that matter, TAN-67 is subsequently converted into a δ opioid receptor *antagonist*! Goodman & Gilman's *The Pharmacological Basis of Therapeutics, 9th Ed.*, McGraw-Hill: NY, 1996, p 549; and Nagase, H., et al., "The Pharmacological Profile of δ Opioid Receptor Ligands, (+) and (-) TAN-67 on Pain Modulation," *Life Sciences*, **2001**, *68*, pp. 2227-2231.



3-(1,2,3,4,4a,5,12,12a-octahydro-2-methylpyrido[3,4-*b*]acridin-4a-yl)phenol (a.k.a. TAN-67)
delta opioid receptor ***agonist***

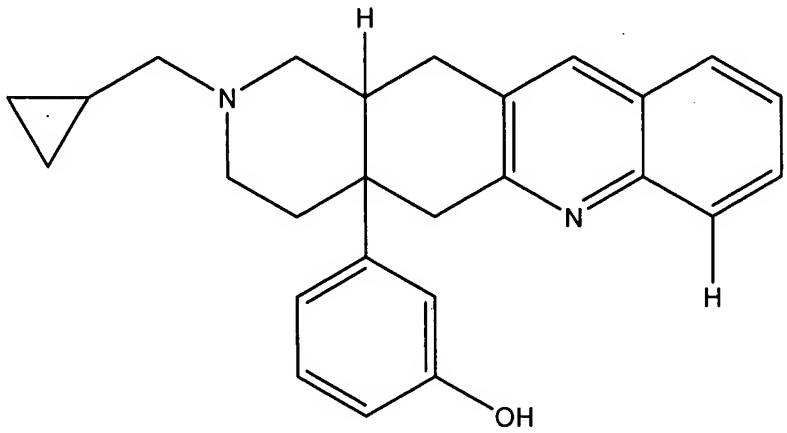


3-(2-(cyclopropylmethyl)-1,2,3,4,4a,5,12,12a-octahydropyrido[3,4-*b*]acridin-4a-yl)phenol
delta opioid receptor ***antagonist***

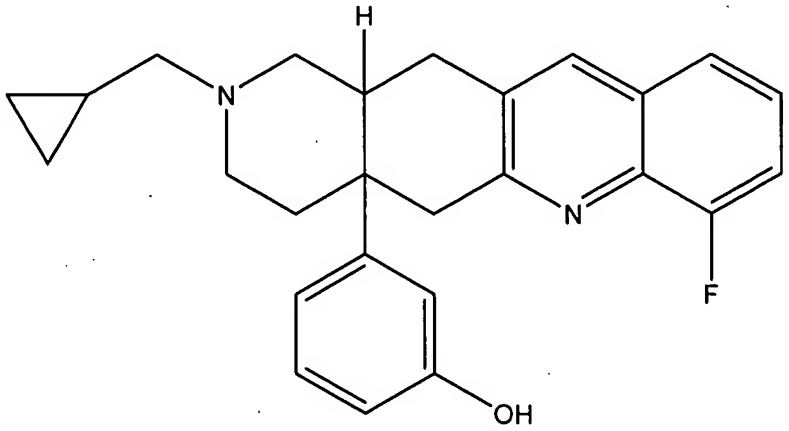


3-(2-allyl-1,2,3,4,4a,5;12,12a-octahydropyrido[3,4-*b*]acridin-4a-yl)phenol
delta opioid receptor ***antagonist***

In addition, if one were to modify the methylcyclopropyl substituted TAN-67, which is a δ opioid receptor *antagonist*, by substituting a fluorine atom for a hydrogen atom on the aromatic phenyl ring near the quinoline nitrogen (shown below), the δ opioid receptor *antagonist* would be converted into a *partial* δ opioid receptor *agonist*, even though fluorine and hydrogen have the comparable atomic radii!

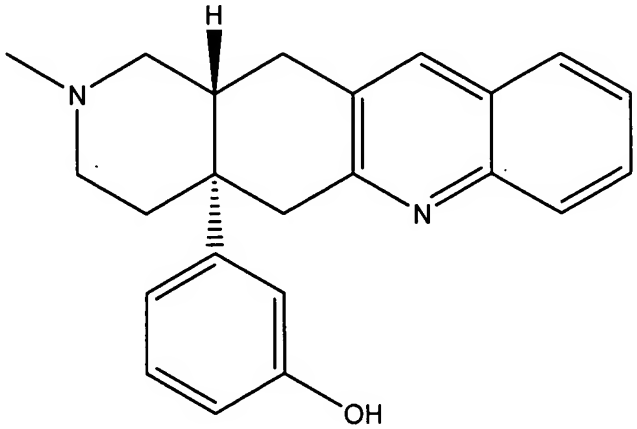


3-(2-(cyclopropylmethyl)-1,2,3,4,4a,5,12,12a-octahydropyrido[3,4-*b*]acridin-4a-yl)phenol
delta opioid receptor ***antagonist***

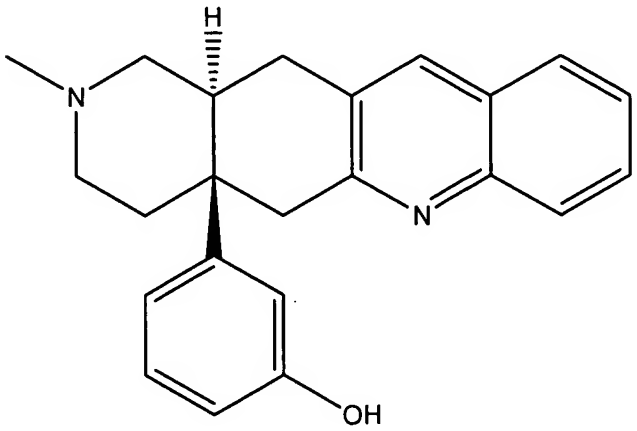


3-(2-(cyclopropylmethyl)-7-fluoro-1,2,3,4,4a,5,12,12a-octahydropyrido[3,4-*b*]acridin-4a-yl)phenol
partial delta opioid receptor ***agonist***

Moreover, by simply selecting from different stereoisomers of TAN-67 (shown below), one could go from (-)TAN-67, which is a potent antinociceptive (analgesic), to (+)TAN-67, which not only fails to exhibit analgesic properties, but astonishingly induces pain-like nociceptive behavior, such as scratching and biting!!!



3-((4a*S*,12a*R*)-1,2,3,4,4a,5,12,12a-octahydro-2-methylpyrido[3,4-*b*]acridin-4a-yl)phenol
(a.k.a. (-)TAN-67)
potent antinociceptive (analgesic)



3-((4a*R*,12a*S*)-1,2,3,4,4a,5,12,12a-octahydro-2-methylpyrido[3,4-*b*]acridin-4a-yl)phenol
(a.k.a. (+)TAN-67)
induces pain-like nociceptive behavior

Based on the aforementioned discussion regarding opioid analgesics, it is readily apparent that minor, seemingly trivial, modifications to the core compound can create profound changes in biological activity. The paramount and unpredictable ramifications that minor structural modifications to the core compound can have on the biological activity of opioid receptors are equally pertinent and applicable to the development of agonists and antagonists of all receptors. Therefore, this example illustrates the exquisite stereospecific characteristics associated with all therapeutic receptor agonists and antagonists.

A final example evidencing unpredictability in association with drug discovery is illustrated by the following research efforts, which utilized combinatorial chemistry techniques. Combinatory chemistry is generally defined as a branch of applied chemistry concerned with the rapid synthesis and screening of large numbers of different but related chemical compounds generated from a known building block in order to recover new substances optimally suited for a specific function. In this particular example, combinatorial chemistry techniques were implemented in an effort to identify more efficacious inhibitors of cathepsin D, which is an aspartyl protease. Kick, E.K., et al., "Structure-Based Design and Combinatorial Chemistry Yield Low Nanomolar Inhibitors of Cathepsin D," *Chemistry & Biology*, **1997**, *4(4)*, pp. 297-307. More specifically, combinatorial libraries were designed and created around the synthesis and subsequent structural derivatization of a stable mimetic building block of the tetrahedral intermediate of amide hydrolysis, namely (hydroxyethyl)amine isostere, which was an already known inhibitor of aspartyl proteases. Of the 2,000 derivatives that comprised the resultant and expansive library, over 90% of the synthesized compounds were biologically *inactive*. Since more than 90% of the synthesized compounds generated in the aforementioned combinatorial

library, which was designed and created around the structural derivatization of a stable and efficacious building block or active core, were in fact biologically *inactive*, one of ordinary skill in the art would have a justifiably sound reason to doubt that even a reasonable fraction, much less a simple majority, of the chemical derivatives disclosed across the entire scope of the tremendously broad and extremely generic claims would in fact possess desired biological activity. With such a high degree of unpredictability in the drug discovery art, the applicant bears a greater burden of providing adequate support in the specification so as to guide one of ordinary skill in the art through the generic maze that is commensurate in scope with the claims.

In the instant case, it has been shown that the presence of a cytosine moiety is not a guarantee of activity against all kinds of cancer. See the discussion regarding Dvonch et al. on page 4 of this office action. It has also been demonstrated that it is generally accepted within the pharmaceutical and drug discovery arts that there is considerable uncertainty regarding the effect of modifications to an active core chemical structure on the observed biological activity of potential therapeutic agents.

The inventor only provides guidance in the specification regarding the treatment of leukemia, colon tumors, melanoma, and CNS, ovarian, renal, prostate, breast, and non-small cell lung cancers, wherein R_1 and R_2 of the administered pharmaceutical **are both hydrogen**. The inventor **does not** provide guidance regarding compounds having other possible substituents for R_1 and R_2 nor does the inventor provide guidance as to which of these many compounds should be used to treat specific cancer types. As described previously, a person of ordinary skill in the art would not know which chemotherapeutic of the many possibilities based on the core structure

provided by the applicant would be appropriate to treat these different cancers without undergoing burdensome undue experimentation.

The inventor provides working examples for the synthesis of several analogs of based upon the core structure depicted on page 4 of this office action, as well as for the administration of (-)-OddC (both R_1 and R_2 are hydrogen) to treat leukemia, colon tumors, melanoma, and CNS, ovarian, renal, prostate, breast, and non-small cell lung cancers.

As discussed previously, the determination of which derivatives of the parent core structure (i.e. (-)-OddC) are effective chemotherapeutics cannot be done based on predictive models, due to the considerable uncertainty present in the pharmaceutical and drug discovery arts regarding modifications of an active core structure and the resulting observed biological activity. The core structure and its derivatives constitute an extremely large genus, which is estimated to comprise at least ~3.8×10^{215} compounds. The uncertainty in the structure function relationships of pharmaceutical agents would impart a burdensome obligation of undue experimentation upon the skilled artisan to ascertain which derivatives provide effective activity against the many different kinds of cancer claimed by the Applicant. This burden is further enhanced by the knowledge that several of the cancers generically claimed (e.g., lymphoma, lung, and head and neck cancer) encompass many different kinds of cancer having distinct points of origin.

Therefore, the examiner concludes that the treatments of leukemia, colon tumors, melanoma, and CNS, ovarian, renal, prostate, breast, and non-small cell lung cancers, wherein R_1 and R_2 of the administered pharmaceutical **are both hydrogen** are enabled, however, the specification does not reasonably provide enablement for head and neck, bladder, uterine, and

small cell lung cancers or for the enabled cancers regarding the administration of the chemotherapeutics of the instant invention **wherein R_1 and R_2 are not both hydrogen**.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 21-23 and 29 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 3-6, and 9-15 of prior U.S. Patent No. 5,817,667 (Chu et al.). This is a double patenting rejection.

It is noted that the medical definitions of the terms (1) tumor and (2) cancer according to the online Medline Merriam Webster Medical Dictionary are the following: (1) an abnormal benign or malignant new growth of tissue that possesses no physiological function and arises from uncontrolled usually rapid cellular proliferation; and (2a) a **malignant tumor** of potentially unlimited growth that expands locally by invasion and systematically by metastasis or (2b) an abnormal state marked by a cancer. From these definitions, one must conclude that all cancers are tumorous, but that not all tumors are cancerous.

Independent claim 20 of the instant application and the relevant dependent claims (21-23 and 29) are drawn to methods of treating different cancers by administration of cytosine-based

compounds and/or their derivatives (see structure on page 4 of this office action). The relevant cancers for rejection of claims 21-23 and 29 are leukemia and cancers of the prostate, lung, and colon.

The claims of U.S. patent '667 are drawn to methods for treating tumors involving administration of the same therapeutic agents claimed in the instant application. Although independent claim 1 is drawn to a method of treating tumors, this claim is further limited by claims 3-6 for the treatment of **cancerous tumors** wherein the cancer is leukemia, prostate cancer, lung cancer, or colon cancer. Claims 9-15 of U.S. patent '667 have similar limitations regarding the kind of cancerous tumors treated as claims 3-6. Independent claim 17 of U.S. patent '667 is drawn to the treatment of cancer by administration of the same chemotherapeutics of the instant application.

Therefore claims 20-23 and 29 of the instant application are coextensive in scope with claims 1, 3-6, and 9-15 of U.S. patent 5,816,667 (Chu et al.), because all cancers are tumorous, per the accepted medical definitions of cancer and tumor.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 5,817,667. Although the conflicting claims are not identical, they are not patentably distinct from each other because the both claim sets are drawn to methods of treating cancer by the administration of the same group of chemotherapeutic compounds.

Claims 21-23 and 29 of the instant application have been discussed above, and if the interpretation of these claims leads one to conclude that they do not reside under the purview of statutory double patenting, they most assuredly fall under the umbrella of obvious type double-patenting. Analysis of claims 20, 24-28, and 30-39 follows.

Independent claims 20 and 30 of the instant application are drawn to a method of treating cancers, including leukemia, lung cancer, prostate cancer, and colon cancer in animals (Claim 20) and humans (Claim 30) by administration of cytosine-based derivatives (see the general formula on page 4 of this action). Although claim 1 of U.S. patent '667 is drawn to the treatment of tumors in animals, it is noted that all cancers are tumorous and that humans are animals. Independent claim 1 of U.S. patent '667 is further limited to humans (dependent claim 2) and to the treatment of cancerous tumors wherein the cancer is prostate cancer, leukemia, colon cancer, and lung cancer (see dependent claims 3-6 and 10-15 of U.S. patent '667). It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to apply the methods disclosed in '667 (claims 1-19), which encompass the same cytosine compounds of the instant invention, to the treatment of cancers, because all cancers are tumorous and humans are animals.

Independent claim 17 of U.S. patent '667 is drawn to a method of treating cancer by administration of the same chemotherapeutics of the instant application. It would have been obvious to a person of ordinary skill in the art to apply the method of claim 17 to the treatment of specific cancers mentioned in earlier claims 3-6 and 9-15 to a host animal or a human, in light of claim 2, as well as to other types of cancers mentioned in claims 24-29 and 34-39. Therefore, a person of ordinary skill in the art would have considered claims 20-39 of the instant application as being *prima facie* obvious in scope with the claims of U.S. patent '667.

Conclusion

Claims 20-39 are rejected. No claims are allowed.

Other Matter

The NPL documents listed in the IDS submitted by the Applicant on March 3, 2004 were not considered, because these documents are no longer available in electronic form for the instant application nor as hard copies in the file wrapper of the parent application (Serial Number: 08/390,633). The examiner respectfully requests that the Applicants resubmit the NPL documents that they would like considered.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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A.U. 1616